POSTER SESSION I

**AUTOLOGOUS TRANSPLANTS**

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### Second Autologous Stem Cell Transplant- an Effective Therapy for Relapsed Multiple Myeloma

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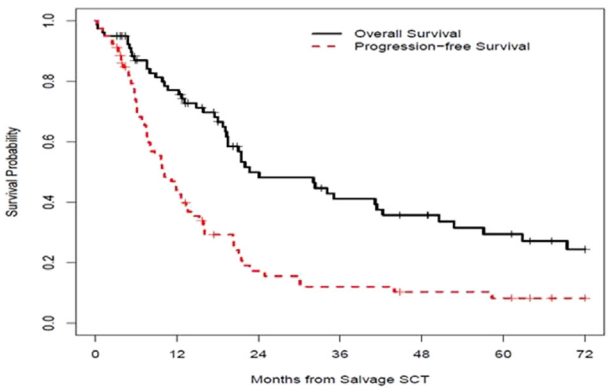
**Background:** Therapeutic options for patients with Multiple myeloma (MM) whose disease has relapsed after a prior autologous stem cell transplant (SCT) include an expanding armamentarium of novel agents, often combined with traditional chemotherapy, or a second SCT, with no clear standard of care.

**Methods:** We retrospectively analyzed the outcomes of patients who underwent salvage melphalan-based SCT for relapsed MM at Memorial Sloan-Kettering Cancer Center.

**Results:** Between 1995 and 2012, 75 patients with MM received an initial SCT and then second autograft for relapsed disease at our center. Conditioning was with melphalan 200mg/m2 (N=43), 180mg/m2 (N=1), 140mg/m2 (N=22), 100mg/m2 (N=9). The median age at 2nd SCT was 59 years (range 36-75) and 58% (N=35) were male. Of those with available data, 35% had high risk cytogenetics (including t (4;14), +1q, p53 loss or del 13q by karyotype) at the time of second SCT. Median interval between first and salvage SCT was 38 months (range 7 -113). Of 71 evaluable patients, 73% had chemotherapy sensitive disease prior to salvage SCT and 27% were chemoresistant. Response was assessed at 2-3 mos post-SCT and 84% of evaluable patients achieved >= partial response (PR), 10% had stable disease (SD), and 7% progressed despite salvage SCT. Following salvage SCT, 37 patients received maintenance therapy and 15 went on to allogeneic SCT. The median PFS following second autograft was 10.1 mos (95% CI: 7.9-13.6); the median OS was 24 mos (95% CI: 19.5 – 50.5). Patients with chemosensitive relapse had better progression free survival (HR-0.51, CI: 0.22-0.77, $P = .005$) and overall survival (HR=0.37, CI- 0.19-0.70, $P = .002$) than patients with resistant relapse. Those with high-risk cytogenetics at the time of second SCT had higher risk of death (HR 2.12, 95% CI: 1.03- 4.38, $P = .04$) compared to patients with standard risk cytogenetics.

**Conclusions:** Salvage SCT is an effective strategy for relapsed MM with chemosensitive disease and results in comparable PFS and OS to other salvage strategies. With the FDA approval of multiple novel effective therapies, more relapsed patients will likely achieve measurable responses and should be evaluated for second stem cell transplant. Incorporation of novel conditioning regimens and/or effective maintenance strategies may further improve outcomes with this approach

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### Cytomegalovirus Reactivation Following Autologous Peripheral Blood Stem Cell Transplantation for Lymphoma and Multiple Myeloma, Single Center Experience

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**Introduction:** There are few s studies about cytomegalovirus reactivation after autologous peripheral blood stem cell transplantation (PBSCT).

**Methods:** At our center we retrospectively reviewed the files for all adult patients with diagnosis of lymphoma or multiple myeloma (MM), who underwent autologous PBSCT between 2007-2012.

All these patients were on acyclovir or valacyclovir prophylaxis, CMV pp65 antigenemia testing was performed weekly till day 40 post transplant, and preemptive therapy was started if the antigenemia test was positive in 5 cells, or more than once positive<5 cells plus unexplained low counts, or elevated liver enzymes.

**Results:** During the six years period, 210 patients underwent autologous transplant (lymphoma 55%, MM45%).97.6% of the patients were CMV IgG positive before transplant.

The rate of CMV reactivation requiring preemptive therapy as per the criteria above was 17.6%, with median time for reactivation of 31 days.

There was no difference in the rate of reactivation between lymphoma and MM, and lymphoma.

Ganciclovir was used as first line therapy in 70.3%, Valganciclovir in 24.3% and Foscarnet in 5.4%. The median duration of induction therapy was 8 days and for maintenance was 10 days.

None of our patients developed CMV disease in any organ, and the main toxicity was cytopenia with the Ganciclovir/Vaganciclovir, and renal impairment with electrolytes imbalance with Foscarnet.

At the time of the study 76% of the group were alive, with 55% were free of progression.

**Conclusion:** CMV reactivation rate is low after autologous PBSCT, no need for CMV monitoring beyond 40 days, and with preemptive therapy you can eradicate CMV infection.

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### PK-Directed Intravenous Busulfan in Combination with High-Dose Melphalan and Bortezomib As Conditioning Regimen for Patients with Multiple Myeloma

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**Introduction:** High dose therapy followed by autologous hematopoietic stem cell transplantation (ASCT) has an established role in the treatment of patients with multiple myeloma (MM). The CR rate, an indicator for progression-free and overall survival (PFS; OS) observed after the most commonly used conditioning regimen Mel200 (Melphalan 200mg/m$^2$) is between 10-35%. The objective of our trial is to assess whether conditioning with a combination of PK-directed Busulfan (Bu), Mel and Bortezomib (Btz) is safe and can improve CR rates in patients with MM.

**Methods:** Patients aged 18-72 with MM, who had received less than one year of prior myeloma-directed therapy and were eligible for ASCT were assigned to receive PK-directed i.v. Bu, i.v. Mel and i.v. Btz as per Fig. 1. Subsequent consolidative or maintenance therapy was left to investigator's choice. Primary outcome was CR rate assessed on D +100 post ASCT as per IMWG criteria. Secondary outcomes are overall response rate (ORR), toxicities, PFS and OS. The trial is registered at clinicaltrials.gov (NCT01605032).

**Results:** To date, 18 patients have been treated (median age 61 (range 44-70), 61% male, 17% with ISS stage 3; median number of prior regimens 1 (range 1-3); prior bortezomib 94%). For the 12 evaluable patients the median days to ANC >/=0.5 x 10$^9$/L and platelet count >/=30 x 10$^9$/L were 11 (range 10-13) and 17 (11-29), respectively. The most common non-hematological toxicities (100%) were alopecia, oral mucositis (62% G3), dysphagia (85% G3), as well as electrolyte abnormalities (62% ≥G3). Other common toxicities were nausea (92%, all G1/2), diarrhea (84% G1/2, 15% G3), while 84% of patients developed fully reversible transaminitis (15% G3). Less common G3 toxicities included delirium (8%), colitis (8%), skin infection (15%; zoster & skin abscess, 1 each), other infections (31%), and engraftment syndrome (8%). No patient developed sinusoidal obstruction syndrome of the liver. Response assessment was available for 11 patients: 1 achieved a stringent CR (9.1%), 5 VGPR (45.5%), and 5 PR (45.5%), resulting in a 100% ORR. After a median follow up of 5.2 months (range 1-18) all patients are alive and no patient has relapsed. The trial is ongoing.

**Conclusion:** PK directed i.v. Bu in combination with Mel and Btz (BuMelBtz) is an effective and safe conditioning regimen for patients with MM. Further evaluation is warranted.

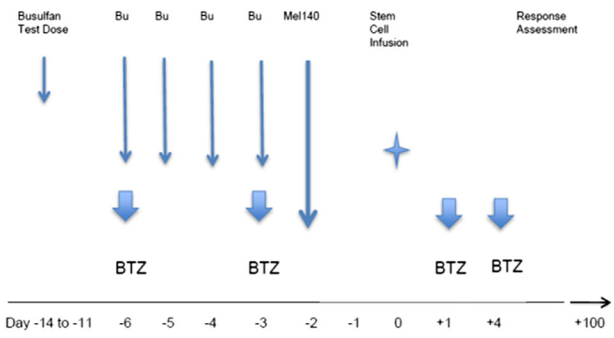


**Fig. 1. Treatment Schema**
Following a Busulfan (Bu) test dose (0.8mg/kg) prior to the first treatment dose, intravenous (i.v.) Bu is given 4 times daily as 3-hour infusion from day (D) -6 to -3 to target a total AUC of 20,000 uMxmin (PK-directed Busulan); i.v. Melphalan (Mel; 140mg/m2) is given on D-2, and i.v. Bortezomib (BTZ; 1.4mg/m2) on D-6, -4, +1 and +4.

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## Chemosensitivity to Induction or High Dose Therapy, Pre/Post Transplant PET Negativity and Absence of Minimal Residual Disease within Mobilized Stem Cell Graft Predict Long Term Disease Free Survival in Multiple Myeloma

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Despite the improvements in response rates in multiple myeloma during the last decade, relapses still remain as a problem. Aim of this study was to evaluate the factors associated with response and the length of progression free survival (PFS) following autologous hematopoietic cell transplantation (ASCT). Out of 113 consecutive patients with newly diagnosed MM, 43 % and 19% achieved Post-ASCT complete remission (CR) or very good partial remission (VGPR) respectively. Post-ASCT response status was significantly associated with female sex, light chain myeloma, β-2 microglobulin (≤3.5mg/L) and pre-ASCT response status. Multiparameter flow cytometry detected abnormal plasma cells (APC) in the harvests of 9.7% of patients. Higher proportion of patients who had contaminated harvests were at <VGPR status during mobilization compared to patients who did not have contamination (73% vs 53%; p=.088). Presence of APC in the harvests compared to those lacking APC was significantly associated with progression at 12 months after ASCT (75% vs 36%; p=.039). The median PFS was 13 (2-45) months after a median follow-up of 33 (7-148) months.

**Table**
Factors Affecting the Post-transplant Progression Free Survival

| | PFS (months) mean ±SD | 95% CI | *P* |
|---|---|---|---|
| Sex | 26.1 ± 2.6 | 21.0-31.2 | .135 |
| Female | 20.3 ± 2.2 | 16.0-24.5 | |
| **Male** | | | |
| Subtype | 30.6 ± 3.0 | 24.7-36.5 | .008 |
| Light chain | 20.3 ± 1.9 | 16.5-24.1 | |
| Others | | | |
| International Staging System | 27.2 ± 2.8 | 21.7-32.7 | .047 |
| ISS1 | 24.2 ± 2.9 | 18.6-29.9 | |
| ISS2 | 15.9 ± 2.7 | 10.7-21.1 | |
| ISS3 | | | |
| Cytogenetics | 24.0 ± 3.1 | 18.1-30.0 | .101 |
| del13q negative | 14.5 ± 2.5 | 9.4-19.5 | |
| del13q positive | | | |
| β 2 microglobulin, mg/L | 25.7 ± 2.7 | 20.5-30.9 | .230 |
| ≤3.5 | 20.9 ± 2.2 | 16.5-25.2 | |
| >3.5 | | | |
| Post-transplant PET | 30.1 ± 3.2 | 23.9-36.3 | .008 |
| Negative | 17.8 ± 2.6 | 12.7-22.8 | |
| Positive | | | |
| APC in harvests | 24.0 ± 1.9 | 20.4-27.7 | .206 |
| Absent | 14.4 ± 3.3 | 8.0-20.8 | |
| Present | | | |
| Pre-transplant response | 14.8 ± 3.8 | 7.3-22.2 | .021 |
| <PR | 19.9 ± 2.5 | 15.0-24.8 | |
| PR | 28.2 ± 4.3 | 19.8-36.7 | |
| VGPR | 28.4 ± 2.8 | 22.8-33.9 | |
| CR | | | |
| Post-transplant response | 3.2 ± 1.2 | 0.85-5.55 | .001 |
| <PR | 17.1 ± 2.8 | 11.6-22.6 | |
| PR | 30.9 ± 3.7 | 23.7-38.0 | |
| VGPR | 26.9 ± 1.8 | 19.8-26.7 | |
| CR | | | |